IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NANOSTRING TECHNOLOGIES, INC., Plaintiff, v. 10X GENOMICS, INC., Defendant.	C.A. No. 22-1375-MFK **JURY TRIAL DEMANDED**

10X GENOMICS, INC.'S ANSWER, DEFENSES,
AND COUNTERCLAIMS TO NANOSTRING'S FIRST AMENDED COMPLAINT

10x Genomics, Inc. ("10x") hereby answers the allegations in NanoString Technologies, Inc.'s First Amended Complaint (D.I. 25) ("FAC"). Unless expressly admitted, 10x denies each and every allegation in NanoString's FAC. To the extent that any non-numbered statements in the FAC contain allegations, 10x denies each and every such allegation.

NANOSTRING'S ALLEGATIONS

NANOSTRING'S ALLEGATIONS RE: NATURE OF THE ACTION

1. 10x admits that NanoString's FAC purports to state a cause of action for infringement of U.S. Patent Nos. 11,473,142 (the "142 Patent") and 11,377,689 (the "689 Patent") (collectively, the "Asserted Patents") arising under the Patent Laws of the United States, 35 U.S.C. § 271. Except as so admitted, 10x denies any remaining allegations of this paragraph.

NANOSTRING'S ALLEGATIONS RE: THE PARTIES

2. Admitted.

3. Admitted.

NANOSTRING'S ALLEGATIONS RE: JURISDICTION AND VENUE

4. 10x incorporates by reference and restates its answers to paragraphs 1-3 of NanoString's FAC as though fully set forth herein.

5. 10x admits that NanoString's FAC purports to state a cause of action for infringement of the Asserted Patents arising under the Patent Laws of the United States, 35 U.S.C. § 271. Except as so admitted, 10x denies any remaining allegations of this paragraph.

6. This paragraph states a legal conclusion to which no response is required. To the extent that a response is required, 10x admits that the Court has subject matter jurisdiction over NanoString's Counts I and II pursuant to U.S.C. §§ 1331 and 1338(a).

7. This paragraph states a legal conclusion to which no response is required. To the extent that a response is required, 10x admits that it is a Delaware corporation and that this Court has personal jurisdiction over 10x for purposes of this action. Except as so admitted, 10x denies the remaining allegations of this paragraph.

8. This paragraph states a legal conclusion to which no response is required. To the extent that a response is required, 10x admits that it is a Delaware corporation and that venue is proper in this Court pursuant to 28 U.S.C. §§ 1391 and 1400(b) for purposes of this action. Except as so admitted, 10x denies the remaining allegations of this paragraph.

NANOSTRING'S BACKGROUND ALLEGATIONS

9. 10x lacks sufficient knowledge or information to form a belief as to whether "GeoMx DSP has been amply described" or whether "studies performed using GeoMx DSP have been widely presented at industry conferences," and on that basis denies the allegations. 10x denies the remaining allegations of this paragraph.

10. 10x admits that Exhibit 1 appears to be an uncertified copy of the 142 Patent, titled "Chemical Compositions and Uses Thereof," which states on its face that it was issued on October

18, 2022, and states on its face that Joseph Beechem, Dae Kim, Margaret Hoang, Mark Gregory, and Erin Piazza are among the alleged inventors. This paragraph states legal conclusions to which no response is required. Except as so admitted, 10x denies the remaining allegations of this paragraph.

11. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x lacks sufficient knowledge or information to form a belief as to the truth of these allegations and on that basis denies them.

12. 10x admits that Exhibit 2 appears to be an uncertified copy of the 689 Patent, titled "Chemical Compositions and Uses Thereof," which states on its face that it was issued on July 5, 2022, and states on its face that Joseph Beechem, Dae Kim, Margaret Hoang, Mark Gregory, and Erin Piazza and Denise Zhou are among the alleged inventors. This paragraph states legal conclusions to which no response is required. Except as so admitted, 10x denies the remaining allegations of this paragraph.

13. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x lacks sufficient knowledge or information to form a belief as to the truth of these allegations and on that basis denies them.

14. 10x admits that the Abstract of each of the Asserted Patent states that it "relates to, among other things, probes, compositions, methods, and kits for simultaneous, multiplexed detection and quantification of protein and/or nucleic acid expression in a user-defined region of a tissue, user-defined cell, and/or user-defined subcellular structure within a cell that are adaptable for use with existing sequencing technologies." Except as so admitted, 10x denies the remaining allegations of this paragraph.

15. 10x admits that the 142 Patent at 1:25-27 and the 689 Patent at 1:25-27 state that "[s]tandard immunohistochemical and in situ hybridization methods allow for simultaneous detection of, at most, six to ten protein or nucleic acid targets." 10x admits that the 142 Patent at 16:30-32 and the 689 Patent at 16:30-32 state that "[s]tandard immunohistochemical methods allow for maximal simultaneous detection of six to ten protein." 10x admits that the 142 Patent at 16:35-37 states that "in situ hybridization methods are limited to simultaneous detection of fewer than ten nucleic acid targets." 10x admits the 142 Patent at 16:37-43 and the 689 Patent at 16:37-43 state that the "present disclosure provides detection of large combinations of nucleic acid targets and/or protein targets from a defined region of a sample. The present disclosure provides an increase in objective measurements by digital quantification and increased reliability and consistency, thereby enabling comparison of results among multiple centers." 10x admits that the 142 Patent at 16:21-23 and 689 Patent at 16:21-23 state that "[t]here is no pre-defined upper limit to the number of regions of interest and comparisons that can be made" and the 142 Patent at 40:65-41:3 and 689 Patent at 40:61-64 state that "1000 or more targets … are detected." 10x admits that the 142 Patent at 37:58-63 and 689 Patent at 37:50-55 state that it "allows economical and rapid flexibility in an assay design, as the target (present in a sample)-specific components of the assay are included in inexpensive and widely-available synthetic DNA oligonucleotides rather than the more expensive probes." Except as so admitted, this paragraph contains allegations that are not "simple, concise, and direct" as required by Federal Rule of Civil Procedure 8(d)(1) and on that basis 10x denies them. Except as so admitted, 10x denies the remaining allegations of this paragraph.

16. 10x admits that it launched and began shipping its first Visium Spatial Gene Expression Solution product in November 2019. 10x lacks sufficient knowledge or information to

form a belief as to what NanoString means by "[10x's] commercial spatial profiling products, Visium Spatial system ("Visium") and related products" and on that basis denies the allegations. Except as so admitted, 10x denies the remaining allegations of this paragraph.

17. 10x admits that it makes, uses, offers for sale, sells, and/or imports Visium CytAssist, Visium Spatial Gene Expression slides, Visium Spatial Gene Expression reagents, and Space Ranger and Loupe Browser in the United States. 10x admits that Space Ranger is analysis software for Visium Spatial Gene Expression experiments for supported libraries. 10x admits that Loupe Browser is visualization software. 10x admits that Visium Spatial Gene Expression Solution allows researchers to "map the whole transcriptome within the tissue context" and "[c]ombine histological and gene expression data with easy-to-use software." *See* https://www.10xgenomics.com/products/spatial-gene-expression. 10x lacks sufficient knowledge or information to form a belief as to what NanoString means by "Visium and related products" and "when used together allow researchers" and on that basis denies the allegations of this paragraph. This paragraph states legal conclusions to which no response is required. Except as so admitted, 10x denies the remaining allegations of this paragraph.

18. 10x admits that use of Visium Spatial Gene Expression provides spatial profiling for RNA in a tissue sample. 10x lacks sufficient knowledge or information to form a belief as to what NanoString means by "10x offers," "workflows that are compatible with standard next generation sequencing (NGS) applications," and "Visium and related products" and on that basis denies the allegations of this paragraph. 10x admits, as stated in its Visium Spatial Gene Expression Product Sheet (https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT059_ProductSheet_VisiumSpatialGeneExpression_Letter_digital.pdf) and in that context, that one can, "[w]ith whole transcriptome analysis, discover and reveal the spatial

organization of cell types, states, and biomarkers." 10x admits, as stated in its Visium Spatial Gene Expression Product Sheet for FFPE (https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT000128_PS_Spatial_biology_without_limits_Spatial_gene_expression_in_FFPE.pdf) and in that context, that with Visium Spatial Gene Expression for FFPE one can "[s]patially profile RNA expression for over 18,000 genes in human and mouse FFPE samples with high resolution across entire tissue sections." 10x admits, as shown on its Visium Spatial Proteogenomics product webpage (https://www.10xgenomics.com/products/spatial-proteogenomics) and in that context, 10x offers "tissue profiling with transcriptomics and protein co-detection." 10x admits, as stated in its Visium Spatial Gene and Protein Expression Product sheet (https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT088_RevA_ProductSheet_Immunofluorescence%20Capability_Letter_digital.pdf) and in that context, that Visium Gene Expression with Immunofluorescence offers a solution allowing users to "[b]roaden [their] reach beyond predefined regions of interest" and allows users to "gain the ability to define regions of interest after [they] have all the data, so as not to miss out on important or unexpected biological results." 10x admits that as stated in its Visium Spatial Gene and Protein Expression Product sheet (https://pages.10xgenomics.com/rs/446-PBO-704/images/10x_LIT088_RevA_ProductSheet_Immunofluorescence%20Capability_Letter_digital.pdf) and in that context, that Visium Gene Expression with Immunofluorescence is "[e]asy to integrate with current histological laboratory methods and tools for tissue analysis." This paragraph states legal conclusions to which no response is required. Except as so admitted, 10x denies the remaining allegations of this paragraph.

19. Denied.

20. Denied.

21. Denied.

22. The allegations of this paragraph are conclusions of law and characterizations of fact to which no response is required. To the extent that a response is required, 10x denies the allegations of this paragraph.

NANOSTRING'S COUNT I

(*Alleged infringement of the 142 Patent*)

23. 10x incorporates and restates by reference its responses to paragraphs 1-22 of NanoString's FAC as through fully set forth herein.

24. Denied.

25. 10x admits that Exhibit 3 is a chart purporting to be an infringement claim chart. 10x lacks sufficient knowledge or information to form a belief as to NanoString's intentions and on that basis denies the allegations in this paragraph. 10x denies that Exhibit 3 is a set of properly formed allegations and on that basis denies the allegations in this paragraph. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x denies the remaining allegations in this paragraph.

26. Denied.

27. Denied.

28. 10x admits that its litigation counsel was aware since at least the October 12, 2022, deposition of Margaret Hoang of U.S. Patent Publication 2021/0403999, which says on its face was published December 30, 2021, and that 10x's litigation counsel questioned Margaret Hoang about it. 10x admits that since October 18, 2022, it was aware of the 142 Patent. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x denies the remaining allegations in this paragraph.

29. Denied.

30. Denied.

NANOSTRING'S COUNT II

(Alleged infringement of the 689 Patent)

31. 10x incorporates and restates by reference its responses to paragraphs 1-30 of NanoString's FAC as through fully set forth herein.

32. Denied.

33. 10x admits that Exhibit 4 is a chart purporting to be an infringement claim chart. 10x lacks sufficient knowledge or information to form a belief as to NanoString's intentions and on that basis denies the allegations in this paragraph. 10x denies that Exhibit 4 is a set of properly formed allegations and on that basis denies the allegations in this paragraph. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x denies the remaining allegations in this paragraph.

34. Denied.

35. Denied.

36. 10x admits that its litigation counsel was aware since at least the July 11, 2022, of NanoString's intent to add a counterclaim of infringement of U.S Patent 11,377,689 to the 22-cv-261 litigation. 10x admits that its litigation counsel received NanoString's proposed amended counterclaims and claim chart applying the 689 Patent to 10x's products, on July 19, 2022. This paragraph states legal conclusions to which no response is required. To the extent that a response is required, 10x denies the remaining allegations in this paragraph.

37. Denied.

38. Denied.

10X'S DEFENSES TO NANOSTRING'S COUNT I & II

By listing any matter as a defense herein, 10x does not assume the burden of proving any matter about which NanoString, or any other party, bears the burden of proof under applicable law.

10X'S FIRST DEFENSE—FAILURE TO STATE A CLAIM

NanoString fails to state a claim upon which relief can be granted.

10X'S SECOND DEFENSE—NON-INFRINGEMENT

10x has not infringed and is not infringing directly, indirectly, or in any other manner any valid and enforceable claim of the Asserted Patents, either literally or under the doctrine of equivalents.

10X'S THIRD DEFENSE—INVALIDITY

The claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to 35 U.S.C. §§ 101, 102, 103, 112, 116, and 282 *et seq*., and the rules, regulations, and laws pertaining to those provisions, including the applicable provisions of Title 37 of the Code of Federal Regulations.

10X'S FOURTH DEFENSE—IMPROPER INVENTORSHIP

As described below, the Asserted Patents are invalid or unenforceable for failing to comply with the requirements for of 35 U.S.C. §§ 101, 116, and 282 because the claims do not name the proper inventor(s).

10X'S FIFTH DEFENSE—LIMITATION ON DAMAGES

NanoString's Asserted Patent infringement claims and Prayer for Relief are limited by 35 U.S.C. § 287.

10X'S SIXTH DEFENSE—ADEQUATE REMEDY AT LAW FOR ALLEGED LIABILITY RELATING TO THE ASSERTED PATENTS

NanoString is not entitled to equitable relief with respect to the Asserted Patents under any theory because NanoString has not and will not suffer irreparable harm, is not without adequate remedy at law, the balance of the hardships does not favor entry of an injunction, and/or public policy concerns weigh against any equitable relief.

10X'S SEVENTH DEFENSE—NO EXCEPTIONAL CASE

10x has not engaged in any conduct that would make this case exceptional and/or would entitle NanoString to an award of attorneys' fees.

10X'S DECLARATORY JUDGMENT COUNTERCLAIMS

10x hereby alleges declaratory judgment counterclaims against NanoString.

NATURE OF ACTION

1. These are counterclaims for declarations of non-infringement, invalidity, and/or unenforceability of one or more claims of U.S. Patent Nos. 11,473,142 (the "142 Patent") and 11,377,689 (the "689 Patent").

PARTIES

2. 10x is a Delaware corporation with its principal place of business at 6230 Stoneridge Mall Road, Pleasanton, CA 94588.

3. NanoString is a Delaware corporation with its principal place of business at 530 Fairview Ave N, Seattle, WA 98109.

JURISDICTION AND VENUE

4. This is an action for declaratory judgment of non-infringement, invalidity, and unenforceability of the 142 and 689 Patents arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq.* and the Declaratory Judgment Act, 28 U.S.C §§ 2201-2202. An actual case and

controversy exists under the Declaratory Judgment Act because NanoString has sued 10x asserting that the 142 and 689 Patents are valid, enforceable, and infringed by 10x, and 10x denies the allegations.

5. This Court has subject matter jurisdiction over these Counterclaims pursuant to 28 U.S.C. §§ 1331 and 1338(a), in combination with 28 U.S.C. §§ 2201-2202.

6. This Court has personal jurisdiction over NanoString because NanoString is a Delaware corporation and NanoString filed its Complaint and FAC in this action.

7. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391 and 1400(b) because NanoString is a Delaware corporation and NanoString filed its Complaint and FAC in this action.

BACKGROUND

8. In the Background to NanoString's FAC, NanoString alleges that NanoString is the owner of the 142 and 689 Patents.

9. NanoString's Count I expressly accuses 10x of infringing the 142 Patent.

10. As a result of NanoString's actions and statements, including the filing and continued assertion of its Complaint and FAC, an actual and justiciable controversy exists between 10x and NanoString regarding the validity, infringement, and enforceability of the 142 Patent.

11. NanoString's Count II expressly accuses 10x of infringing the 689 Patent.

12. As a result of NanoString's actions and statements, including the filing and continued assertion of its Complaint and FAC and the assertion of the 689 Patent in the 22-cv-261 (Del.) case, an actual and justiciable controversy exists between 10x and NanoString regarding the validity, infringement, and enforceability of the 689 Patent.

13. A judicial declaration and determination are necessary and appropriate at this time given NanoString's allegations and in order that 10x may ascertain its rights and duties with respect to the 142 and 689 Patents.

COUNT I: DECLARATORY JUDGMENT OF

NON-INFRINGEMENT OF U.S. PATENT NO. 11,473,142

14. 10x restates and incorporates by reference the denials, admissions, allegations, and defenses contained in its Answer and Defenses to NanoString's FAC against 10x as if fully set forth herein. 10x further restates and incorporates by reference its allegations in paragraphs 1 through 13 of its Declaratory Judgment Counterclaims.

15. In its Count I, NanoString has expressly accused 10x of infringing the 142 Patent.

16. 10x has not been and is not now infringing, directly or indirectly, literally or under the doctrine of equivalents, or willfully, any valid and enforceable claim of the 142 Patent.

17. 10x does not infringe any valid and enforceable claims of the 142 Patent at least because neither 10x nor anyone else has used or uses 10x's products to practice each and every step of the independent claims of the 142 Patent.

18. For example, as properly construed, the 142 Patent claims require collecting probes or portions thereof from user-defined regions of interest of the tissue sample. In contrast, 10x's products including without limitation Visium Spatial Gene Expression, i.e., the instrumentalities described as meeting the limitations of Claim 1 of the 142 Patent in NanoString's Exhibit 3, are not used to collect probes or portions thereof from user-defined regions of interest of the tissue sample either literally or under the doctrine of equivalents.

19. Additionally, each of the claims of the 142 Patent is invalid and unenforceable as set forth below in Count II of 10x's Declaratory Judgment Counterclaims. An invalid claim cannot be infringed.

20. In view of Count I against 10x, there is an actual controversy between NanoString and 10x regarding the 142 Patent. Accordingly, a valid and justiciable controversy has arisen and exists between NanoString and 10x with respect to the alleged infringement of the 142 Patent. 10x

desires a judicial determination and declaration of the respective rights and duties of the parties herein. Such a determination and declaration are necessary and appropriate so that the parties may ascertain their respective rights and duties.

21. 10x is entitled to a declaratory judgment that: (a) it has not infringed and is not infringing, literally or under the doctrine of equivalents, directly or indirectly, any valid and enforceable claim of the 142 Patent; and (b) it is not liable for any alleged infringement of the 142 Patent.

COUNT II: DECLARATORY JUDGMENT OF INVALIDITY OF U.S. PATENT NO. 11,473,142

22. 10x restates and incorporates by reference the denials, admissions, allegations, and defenses contained in its Answer and Defenses to NanoString's FAC against 10x as if fully set forth herein. 10x further restates and incorporates by reference its allegations in paragraphs 1 through 21 of its Declaratory Judgment Counterclaims.

23. The claims of the 142 Patent are invalid for failure to comply with the conditions of patentability, including but not limited to 35 U.S.C. §§ 101, 102, 103, 112, and/or 115. For example, all claims of the 142 Patent are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of Ståhl *et al.*, "Visualization and analysis of gene expression in tissue sections by spatial transcriptomics," Science Vol. 353, Issue 6294 (2016) ("Ståhl"), which discloses and/or renders obvious all elements of the claims of the 142 Patent.

24. All claims of the 142 Patent are invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the specification of the 142 Patent fails to contain a written description of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of written description support for and lack of

enablement of "collecting a plurality of oligonucleotides" and "spatially detecting the plurality of oligonucleotides collected from the first location . . . ."

25. All claims of the 142 Patent are further invalid and unenforceable for failure to satisfy the requirements of 35 U.S.C. §§ 101, 116, and 282 because the 142 Patent does not name Gordon Mills as an inventor. NanoString describes Gordon Mills' role in inventorship as follows:

> A team at NanoString led by Joe Beechem, our Chief Scientific Officer, was testing a number of protein assay possibilities with oligo-labeled antibodies, therefore they were already equipped for the challenge. …
>
> **We were not quite ready yet to enter the world of spatial transcriptomics.**
>
> He was in his room at the Marriott Hotel, waiting to walk across the street to the MD Anderson Cancer Center when he started thinking: what can we do with antibodies labeled with photocleavable barcoded antibodies that would increase the sensitivity to protein detection that are also spatially resolved? Can we build a microscope or an imaging system to visualize the antibody locations and then use the photocleavable linker to "spatially localize things"? He jotted the idea down on a hotel pad and left to go give his talk.
>
> Later that evening, **Joe was with Gordon Mills, then chair of the Department of Systems Biology at MD Anderson, when he realized they both were thinking of very similar ideas. The two started brainstorming, drawing on a whiteboard to scope out if-and-how such a system would work, and what making such technology would require** . . .

See Exhibit A (https://nanostring.com/blog/pioneers-in-spatial-transcriptomics-the-birth-of-geomx-dsp/) (emphasis added). The 142 Patent should name Gordon Mills at least as co-inventor to the claims of the 142 Patent.

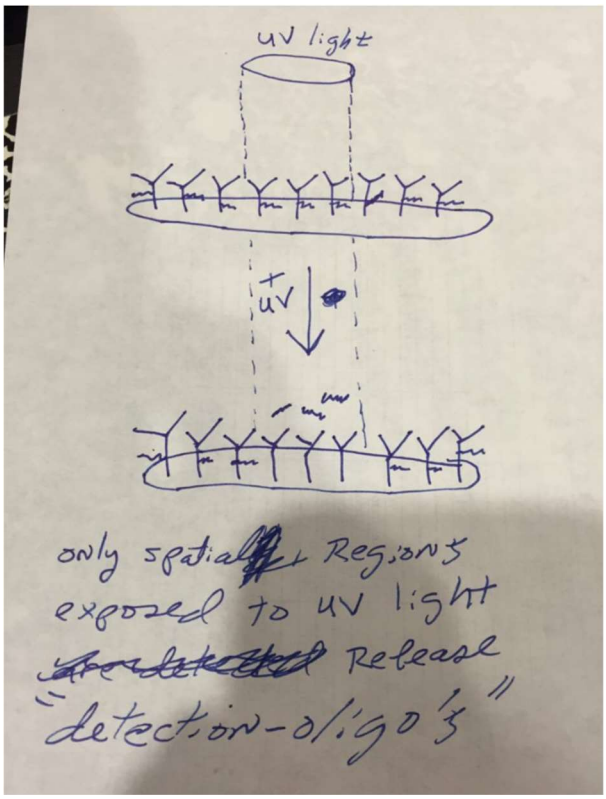
26. The claims of the 142 Patent recite limitations that are allegedly inventive contributions of the inventorship group that NanoString claims conceived of the inventions of US2020/0040385A1 (the "385 Application") and U.S. 10,640,816 (the "816 Patent") that name inventors, such as Gordon Mills and Chris Merritt, who are not named inventors of the 142 Patent. For example, under NanoString's contentions, the 385 Application claims include the same steps claimed in the asserted claims of the 142 Patent, such as "contacting" nucleic acid targets with

probes with target-binding domains, "collecting" portions of probes, and "detecting" the target at a location via sequencing. On information and belief, at least Dr. Gordon Mills and Dr. Chris Merritt are alleged to have participated in the conception of and made substantial, inventive contributions to the methods that are claimed in the 142 Patent under NanoString's contentions, including by contributing the steps of "contacting," "collecting," and "sequencing."

27. The named inventors who were added to the 142 Patent but who were not involved in the conception of the 385 Application are not properly considered joint inventors. For example, under NanoString's apparent contentions, the "extension" steps in the GeoMx workflow are not more than the implementation of common Illumina i5 and i7 sample indexing, without modification or special use for "location." To the extent that any of the named inventors added to the 142 Patent only contributed to recited prior art extension steps, such contribution does not meet the requirements of joint inventorship.

28. In another example, to the extent that NanoString claims that a dual-probe approach is an inventive contribution to the 142 Patent, on information and belief that contribution was not made by any of the named inventors of the 142 Patent.

29. All claims of the 142 Patent are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the specification of the 142 Patent fails to demonstrate that the inventors were in possession of a process beyond collecting portions of probes from user-defined regions of interest of the tissue sample using UV light. *See* Exhibit A at "Napkin":



See also, *e.g.*, 142 Patent at Abstract, 1:28-32; 1:39-42; 16:8-14; 16:37-40; 19:54-62; 22:18-26; 24:16-25; 29:19-27; 32:59-67; 34:20-28; 35:46-54; 40:27-31; 40:38-40; 42:15-17; 42:18-25; 47:58-61.

30. Accordingly, a valid and justiciable controversy has arisen and exists between NanoString and 10x with respect to the validity of the 142 Patent. 10x desires a judicial determination and declaration of the respective rights and duties of the parties herein. Such a determination and declaration are necessary and appropriate so that the parties may ascertain their respective rights and duties.

31. 10x is entitled to a declaratory judgment that the claims of the 142 Patent are invalid or unenforceable.

COUNT III: DECLARATORY JUDGMENT OF NON-INFRINGMENT OF U.S. PATENT NO. 11,377,689

32. 10x restates and incorporates by reference the denials, admissions, allegations, and defenses contained in its Answer and Defenses to NanoString's FAC against 10x as if fully set forth herein. 10x further restates and incorporates by reference its allegations in paragraphs 1 through 31 of its Declaratory Judgment Counterclaims.

33. In its Count II, NanoString has expressly accused 10x of infringing the 689 Patent.

34. 10x has not been and is not now infringing, directly or indirectly, literally or under the doctrine of equivalents, or willfully, any valid and enforceable claim of the 689 Patent.

35. 10x does not infringe any valid and enforceable claims of the 689 Patent at least because neither 10x nor anyone else has used or uses 10x's products to practice each and every step of the independent claims of the 689 Patent.

36. For example, as properly construed, the 689 Patent claims require collecting probes or portions thereof in solution before the incorporation of a nucleic acid sequence that identifies a location of the tissue sample. In contrast, 10x's products including without limitation Visium Spatial Gene Expression for FFPE, i.e., the instrumentalities described as meeting the limitations of Claim 16 of the 689 Patent in NanoString's Exhibit 4, are not used to collect probes or portions thereof in solution either literally or under the doctrine of equivalents.

37. Additionally, as properly construed, the 689 Patent claims require collecting probes or portions thereof from user-defined regions of interest of the tissue sample. In contrast, 10x's products including without limitation Visium Spatial Gene Expression for FFPE, i.e., the instrumentalities described as meeting the limitations of Claim 16 of the 689 Patent in NanoString's Exhibit 4, are not used to collect probes or portions thereof from user-defined regions of interest of the tissue sample either literally or under the doctrine of equivalents.

38. In another example, as properly construed, the 689 Patent claims require application of location-specific forces to release probes or portions thereof from locations in the tissue sample without releasing probes from other locations. In contrast, 10x's products including without limitation Visium Spatial Gene Expression for FFPE, i.e., the instrumentalities described as meeting the limitations of Claim 16 of the 689 Patent in NanoString's Exhibit 4, are not used for applying conditions that release probes from specific locations either literally or under the doctrine of equivalents.

39. In another example, as properly construed, the 689 Patent claims require an extension reaction that incorporates a nucleic acid sequence that identifies a location into each nucleic acid probe. In contrast, 10x's products including without limitation Visium Spatial Gene Expression for FFPE, i.e., the instrumentalities described as meeting the limitations of Claim 16 of the 689 Patent in NanoString's Exhibit 4, are not used to incorporate a nucleic acid sequence that identifies a location into each probe either literally or under the doctrine of equivalents.

40. In another example, as properly construed, the 689 Patent claims require spatially detecting the at least one target analyte in locations of the tissue sample. In contrast, under NanoString's contentions, 10x's products including without limitation Visium Spatial Gene Expression for FFPE, i.e., the instrumentalities described as meeting the limitations of Claim 16 of the 689 Patent in NanoString's Exhibit 4, are not used to spatially detect target analytes at locations in the tissue sample either literally or under the doctrine of equivalents.

41. Additionally, each of the claims of the 689 Patent is invalid and unenforceable as set forth below in Count IV of 10x's Declaratory Judgment Counterclaims. An invalid claim cannot be infringed.

42. In view of Count II against 10x, there is an actual controversy between NanoString and 10x regarding the 689 Patent. Accordingly, a valid and justiciable controversy has arisen and exists between NanoString and 10x with respect to the alleged infringement of the 689 Patent. 10x desires a judicial determination and declaration of the respective rights and duties of the parties herein. Such a determination and declaration are necessary and appropriate so that the parties may ascertain their respective rights and duties.

43. 10x is entitled to a declaratory judgment that: (a) it has not infringed and is not infringing, literally or under the doctrine of equivalents, directly or indirectly, any valid and enforceable claim of the 689 Patent; and (b) it is not liable for any alleged infringement of the 689 Patent.

COUNT IV: DECLARATORY JUDGMENT OF INVALIDITY OF U.S. PATENT NO. 11,377,689

44. 10x restates and incorporates by reference the denials, admissions, allegations, and defenses contained in its Answer and Defenses to NanoString's FAC against 10x as if fully set forth herein. 10x further restates and incorporates by reference its allegations in paragraphs 1 through 43 of its Declaratory Judgment Counterclaims.

45. The claims of the 689 Patent are invalid for failure to comply with the conditions of patentability, including but not limited to 35 U.S.C. §§ 101, 102, 103, 112, and/or 115. For example, all claims of the 689 Patent are invalid under 35 U.S.C. §§ 102 and/or 103 at least in view of U.S. Patent No. 10,961,566 ("Chee"), alone or in combination with additional prior art, including U.S. Patent No. 10,155,981 ("Brenner"), which disclose(s) and/or render obvious all elements of the claims of the 689 Patent.

46. All claims of the 689 Patent are invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the specification of the 689 Patent fails to contain a written description

of the claims or sufficient information to enable a person of ordinary skill in the art to practice the full scope of the claims. For example, there is a lack of written description support for and lack of enablement of "collecting the nucleic acid probes," "conditions that release the nucleic acid probes, or portions thereof," and limitations related to "ligated probes."

47. All claims of the 689 Patent are further invalid and unenforceable for failure to satisfy the requirements of 35 U.S.C. §§ 101, 116, and 282.

48. For example, the 689 Patent does not name Gordon Mills as an inventor. NanoString describes Gordon Mills' role in inventorship as follows:

> A team at NanoString led by Joe Beechem, our Chief Scientific Officer, was testing a number of protein assay possibilities with oligo-labeled antibodies, therefore they were already equipped for the challenge. …
>
> **We were not quite ready yet to enter the world of spatial transcriptomics.**
>
> He was in his room at the Marriott Hotel, waiting to walk across the street to the MD Anderson Cancer Center when he started thinking: what can we do with antibodies labeled with photocleavable barcoded antibodies that would increase the sensitivity to protein detection that are also spatially resolved? Can we build a microscope or an imaging system to visualize the antibody locations and then use the photocleavable linker to "spatially localize things"? He jotted the idea down on a hotel pad and left to go give his talk.
>
> Later that evening, **Joe was with Gordon Mills, then chair of the Department of Systems Biology at MD Anderson, when he realized they both were thinking of very similar ideas. The two started brainstorming, drawing on a whiteboard to scope out if-and-how such a system would work, and what making such technology would require** . . .

See Exhibit A (https://nanostring.com/blog/pioneers-in-spatial-transcriptomics-the-birth-of-geomx-dsp/) (emphasis added). The 689 Patent should name Gordon Mills at least as co-inventor to the claims of the 689 Patent.

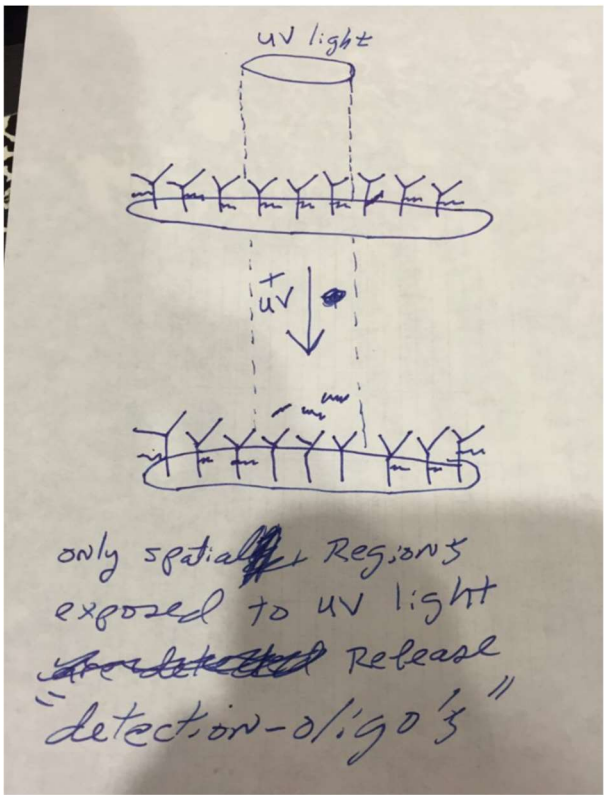
49. The claims of the 689 Patent recite limitations that are allegedly inventive contributions of the inventorship group that NanoString claims conceived of the inventions of the 385 Application and U.S. 10,640,816 that name inventors, such as Gordon Mills and Chris Merritt,

who are not named inventors of the 689 Patent. For example, under NanoString's contentions, the 385 Application claims include the same steps claimed in the asserted claims of the 689 Patent, such as "contacting" nucleic acid targets with probes with target-binding domains, "collecting" portions of probes, and "detecting" the target at a location via sequencing. On information and belief, at least Dr. Gordon Mills and Dr. Chris Merritt are alleged to have participated in the conception of and made substantial, inventive contributions to the methods that are claimed in the 689 Patent under NanoString's contentions, including by contributing the steps of "contacting," "collecting," and "sequencing."

50. The named inventors who were added to the 689 Patent but who were not involved in the conception of the 385 Application are not properly considered joint inventors. For example, under NanoString's apparent contentions, the "extension" steps in the GeoMx workflow are not more than the implementation of common Illumina i5 and i7 sample indexing, without modification or special use for "location." To the extent that any of the named inventors added to the 689 Patent only contributed to recited prior art extension steps, such contribution does not meet the requirements of joint inventorship.

51. In another example, to the extent that NanoString claims that a dual-probe approach is an inventive contribution to the 689 Patent, on information and belief that contribution was not made by any of the named inventors of the 689 Patent.

52. All claims of the 689 Patent are further invalid for failure to satisfy the requirements of 35 U.S.C. § 112. For example, the specification of the 689 Patent fails to demonstrate that the inventors were in possession of a process beyond collecting portions of probes from user-defined regions of interest of the tissue sample using UV light. *See* Exhibit A at "Napkin":



See also, *e.g.*, 689 Patent at Abstract, 1:28-32; 1:39-42; 16:8-14; 16:37-40; 19:54-62; 22:16-24; 24:22-32; 29:22-33; 32:53-62; 34:14-22; 35:41-49; 40:21-25; 40:32-34; 42:10-12; 42:13-20; 47:52-54.

53. Accordingly, a valid and justiciable controversy has arisen and exists between NanoString and 10x with respect to the validity of the 689 Patent. 10x desires a judicial determination and declaration of the respective rights and duties of the parties herein. Such a determination and declaration are necessary and appropriate so that the parties may ascertain their respective rights and duties.

54. 10x is entitled to a declaratory judgment that the claims of the 689 Patent are invalid or unenforceable.

PRAYER FOR RELIEF

10x denies that NanoString is entitled to any relief whatsoever from either 10x or the Court, including the relief requested in paragraphs A-G of NanoString's Prayer for Relief.

10x prays that the Court enter a judgment as follows:

A. That NanoString's claims be dismissed with prejudice and NanoString take nothing;

B. Judgment in favor of 10x for all claims;

C. A declaration that the 142 and 689 Patents are invalid and/or unenforceable;

D. A declaration that 10x has not and does not infringe the 142 and/or 689 Patents;

E. That NanoString be required to pay 10x's attorneys' fees and costs;

F. A declaration that the case is an exceptional case and that NanoString be required to pay 10x's attorneys' fees pursuant to 35 U.S.C. § 285; and

G. A judgment awarding 10x such other and further relief as the Court may deem just, reasonable, and proper.

DEMAND FOR JURY TRIAL

10x acknowledges NanoString's request for a jury trial on its claims and, pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, 10x also demands a jury trial on all issues so triable.

Respectfully Submitted,

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Dated: February 10, 2023

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